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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/692,299	10/22/2003	Napoleone Ferrara	11669.0139USC1	9503

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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 10/692,299	Applicant(s) FERRARA ET AL.	
	Examiner Phuong Huynh	Art Unit 1644	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 12 June 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *6 and 8*.
   Claim(s) objected to: *11*.
   Claim(s) rejected: *1-4, 7, 9-10, and 12*.
   Claim(s) withdrawn from consideration: *13-25*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

Continuation of 11. does NOT place the application in condition for allowance because: the following rejection remains.

Claims 1-4, 7, 9-10 and 12 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a written description of (1) any isolated polypeptide having at least "80%, 85%, 90%, or 95% amino acid sequence identity with the amino acid sequence of residues 20 to 105 of SEQ ID NO: 2, wherein the polypeptide promotes proliferation of adrenal cortex-derived capillary endothelial cells as set forth in claims 1-4, and 7, (2) any isolated polypeptide mentioned above is a native sequence of any endocrine gland-derived vascular endothelial growth factor (EG-VEGF), any allelic variant of any EG-VEGF, or any native human EG-VEGF

The claims encompass any polypeptide that comprise the full-length sequence having at least about 80%, 85%, 90%, 95% identity to amino acid residues 20 to 105 of SEQ ID NO: 2 or any polypeptide that comprise an amino acid sequence having at least about 80%, 85%, 90%, 95% identity to any portion of amino acid residues 20-105 of SEQ ID NO: 2.
The term "EG-VEGF variant polypeptide" as defined in the specification at page 13 is any EG-VEGF having one more amino acid residues are added, or deleted, tat the N- and/or C-terminals as well as within one or more internal domains of SEQ ID NO: 2. The EB-VEGF variant polypeptide does not encompass the native EG-VEGF polypeptide sequence. EG-VEGF variant polypeptides are at least 10 amino acids in length (see page 14). The allelic variant of EG-VEGF will have at least about 80%, 85%, 90% or 95% identity from x to 105 of amino acid of SEQ ID NO: 2 (see page14).

The specification discloses only one isolated polypeptide comprising the amino acid sequence of SEQ ID NO: 2 wherein the polypeptide is a human EG-VEGF for screening agonist or antagonist (page 54-56) and production of antibody that binds specifically to EG-VEGF (See page 65). The mature EG-VEGF has the amino acid residues 20 to 105 of SEQ ID NO: 2. The specification further discloses that EG-VEGF is expressed in the endocrine tissues such as the stroma cell and granulose cells in the ovary, the Leydig cell in the testis, the adrenal gland and the placenta. The EG-VEGF is mitogenic and chemo attractant for specific endothelial cells but not human aortic vascular smooth muscle cells, pericytes, fibroblast, human neonatal fibroblasts and karatinocytes. The angiogenic effect of EG-VEGF is tissue specific since EG-VEGF has no effect on rat corneal pocket assay. The specification further discloses that injection of Adenoviral vector carrying the human EG-VEGF cDNA or VEGF causes an increase in angiogenesis, large fluid-filled or hemorrhagic cystic formation in ovary (Fig. 19).

With the exception of the specific polypeptide mentioned above, there is insufficient written description about the structure associated with function of any and all polypeptide having at least 80%, 85%, 90%, or 95% amino acid sequence idetntity with the amino acid sequence of residues 20 to 105 of SEQ ID NO: 2 wherein the polypeptide promotes proliferation of adrenal cortex-derived capillary endotehlial cells.

The disclosure fails to adequately describe which amino acids within the mature sequence of residues 20 to 105 of SEQ ID NO: 2 to be substituted for which residues, deleted, added and/or combination thereof such that the undiclosed polypeptide still maintains its structure and function.

The specification discloses only human EG-VEGF comprising the amino aid sueqence of SEQ ID NO: 2, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species of allelic variants of EG-VEGF to describe the genus for the claimed polypeptide. Thus, Applicant was not in possession of the claimed genus. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398; University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC2004).
Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 6/12/06 have been fully considered but are not found persuasive.
Applicants' position is that claim 1 as amended is drawn to an isolated EG-VEGF polypeptide having at least 80% amino acid sequence identity with the amino acid sequence of residues 20-105 of SEQ ID NO:2. The language of the claim is consistent with the descliption of EG-VEGF in the specitkation (e.g., at page 13, lines 10-13) and specifies that the claimed polypeptide contains the amino acid sequence of mature EG-VEGF (residues 20-105 of SEQ ID NO:2 or a sequence having at least 80% identity to residues 20-105). EG-VEGF polypeptides having at least 80% amino acid sequence identity with the amino acid sequence of residues 20-105 of SEQ I.D NO:2 are clearly described in the specification. On page 13, "EG-VEGF variant polypeptide" is described as an active EG-VEGF polypeptide having at least about 80% amino acid sequence identity with the amino acid sequence of (a) residues 1 or about 20 to 105 of SEQ ID NO:2, (b) X to 105 of SEQ ID NO:2 wherein X is any amino acid residue from 14 or 24 of SEQ ID NO:2, or (c) another specifically derived fragment of the amino acid sequence of SEQ ID NO:2. As such, one of ordinary skill in the art reading this definition would understand that EG-VEGF variant polypeptides as described in the application fall into three different, albeit related categories. Comparing this definition to the presently amended claim 1, it is apparent that the presently amended claim 1 is directed to a part of category (a) Imder this definition (EG-VEGF variants having at least 80% amino acid sequence identity with the amino acid sequence of residues 20-105 of SEQ ID NO22). In contrast, the Examiner's reading of claim 1 appears to rely on category (b) or (c) of the definition. On page 45, the specification describes valiants of EG-VEGF to include EG-VEGF derived from other species. Also desclibed are nucleic acid probes derived from EG-VEGF useful to identify such variant species. As discussed in the prior response, non-human species of EG-VEGF having at least 80% amino acid sequence identity with the amino acid sequence of residues 20-105 of SEQ ID NO:2 were identified for murine, rat, and bovine species (see Table 1 of the prior response).

In response, the specifcation as filed does not describe any isolated polypeptide having at least "80%, 85%, 90%, or 95% amino acid sequence identity" with the amino acid sequence of residues 20 to 105 of SEQ ID NO: 2 other than human EG-VEGF comprising the amino acid sequence of SEQ ID NO: 2 wherein the polypeptide promotes proliferation of adrenal cortex-derived capillary endothelial cells. The specification as filed does not disclose any EG-VEGF polypeptide from other species such as murine, rat and bovine species or any allelic variants thereof as argued.

The term "EG-VEGF variant polypeptide" as defined in the specification at page 13 is any active EG-VEGF polypeptide having at least about 80% amino acid sequence identity with the amino acid sequence of (a) residues 1 or about 20 to 105 of the EG-VEGF polypeptide shown in Figure 2 (SEQ ID NO:2), (b) X to 105 of the EG-VEGF polypeptide shown in Figure 2 (SEQ ID NO:2), wherein X is any amino acid residue from 14 to 24 of Figure 2 (SEQ ID NO:2), or (c) another specifically derived fragment of the amino acid sequence shown in Figure 2 (SEQ ID NO:2). Such EG-VEGF variant polypeptides include, for instance, EG-VEGF polypeptides wherein one or more amino acid residues are added, or deleted, at the N- and/or C-terminus, as well as within one or more internal domains, of the sequence of Figure 2 (SEQ ID NO:2). The specification does not adequately describe which one or more internal domains of EG-VEGF polypeptide to be deleted, much less the EG-VEGF polypetide having at least 80% amino acid sequence identity with the amino acid residues 20 to 105 of SEQ ID NO: 2 still maintains its structure and function. Accordingly, any isolated polypeptide having at least "80%, 85%, 90%, or 95% amino acid sequence identity" with the amino acid sequence of residues 20 to 105 of SEQ ID NO: 2 and any allelic variant thereof are not adequately described.

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